

Remarks

Claims 1-15 were pending in the present application.

Applicants have canceled claims 1-4, without prejudice, and amended claims 5, 6, and 9-15, without prejudice. Applicants reserve the right to pursue the deleted subject matter in one or more continuing applications.

The claim amendments have been made to clarify that which Applicants regard as the invention, to correct antecedent bases and to correct editorial errors. Specifically, claims 5 and 6 have been amended to clarify that the culture temperature in steps c) and d), respectively, is above the culture temperature in step a). Support for this amendment can be found in the specification, published as U.S. Patent Application Publication No. US 2005/0176146 A1 ("published specification"), for example, at paragraph [0028]. Claims 5 and 6 have been further amended to specify adenovirus throughout the claim for proper antecedent bases. Claim 6 has been yet further amended to correct editorial errors, including correcting the mislabeling of two different steps d). Claims 9-15 have been amended to improve clarity. Specifically, claims 9-15 have been amended to recite that the temperature for cell growth in step b) is from 31°C to 34°C, the temperature for cell growth in step a) is from 35°C to 38°C, and/or the temperature for growth of infected host cells of step c) is from about 35°C to 38°C or from about 36°C to 38°C. Support for these amendments can be found in the published specification, for example, at paragraph [0028].

No new matter has been added by these amendments.

After entry of the amendments, claims 5-15 will be pending.

Applicants respectfully request entry of the foregoing amendments and consideration of the following remarks.

Claim Rejections – 35 U.S.C. § 112

Claims 1-15 were rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse.

The Examiner contends that the metes and bounds of claim 1-8, with respect to the phrases, "at a temperature below a physiological optimum for host cell growth", and "at or near a physiologically optimum temperature for producing virus", cannot be determined.

Definiteness of claim language must be analyzed, not in a vacuum, but in light of:

- (A) The content of the particular application disclosure;
- (B) The teachings of the prior art; and
- (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent. See, e.g., *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000).

MPEP §2173.02

If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph, would be appropriate. See *Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993).

Id.

It is an accepted practice that cell growth in culture is typically conducted at the physiological temperature of 37°C and virus propagation is conducted at the same temperature as cell growth or shifted downward to a lower temperature. See published specification at paragraph [0025]. The present invention is based on a counter-intuitive temperature shift strategy for cell growth which comprises reducing the cell culture temperature to a sub-optimal level for a period of time prior to virus infection or growing cells at a sub-optimal level for the entire cell expansion process including one or more passages of cell growth from cryopreserved cells, followed by a shift up to or near the physiological temperature for production of that particular virus prior to, simultaneous with, or after virus infection of the host cells. See published specification at paragraphs [0010] and [0025]. Examples are provided where the

temperature for suboptimal cell growth is from about 31°C to 35°C and the physiologically optimum temperature range is from about 35°C to 38°C.

The specification notes that the physiological temperature of 37°C has been shown to be optimal for growth of a majority of mammalian cell lines (implying that many mammalian cell lines do not have optimum growth at 37°C). See published specification at paragraph [0006]. The specification also teaches that a return to the physiological temperature depends on the respective host cell and/or virus. See *id.* at paragraph [0028]. It would be routine experimentation to determine the physiologically optimum temperature for the growth of a particular cell line, e.g., by measuring cell counts over time at different temperatures. Based on the determination of a physiologically optimum temperature for a particular cell line, a suitable temperature at or near a physiologically optimum temperature for producing virus can readily be determined and a temperature below a physiologically optimum for host cell growth can "easily be tested by the artisan" using routine experimentation based on the teachings of the specification. See *id.* The specification also notes that the optimal temperature for virus production depends on the virus strain and the host cell line. See published specification, for example, at paragraph [0006].

Thus, the contents of the specification and the teachings of the prior art teach that the metes and bounds of a "temperature below a physiological optimum for host cell growth" and "a temperature at or near a physiologically optimum temperature for producing virus" will vary depending on the specific virus and host cell combination used. However, the metes and bounds can readily be determined by the skilled artisan for any combination of virus and host cell. The present invention is based on a counter intuitive approach of reducing the cell culture temperature to a sub-optimal level and then shifting up to or near the physiological temperature for production. Applicants respectfully submit that, based on the above, the claims sufficiently apprise one of ordinary skill in the art of their scope and provide clear warning to others as to what constitutes infringement of the patent.

The Examiner further contends that claims 9-15 recite temperature ranges that are not clear. Specifically, the Examiner contends that the range encompassed by "from between 31°C and 34°C" is not clear. In an effort to clarify that which Applicants regard as the invention,

Applicants have amended claims 9-15 to recite a temperature range "from 31°C to 34°C."

Applicants believe that the claims as amended clearly set forth that the specified temperature is in the range of 31°C to 34°C.

The Examiner further contends that claims 14 and 15 are not clear in reciting the limitation "and the temperature for growth of infected host cells of step c) is from about 36°C and 38°C". Applicants have amended claims 14 and 15 to recite a temperature range "from 36°C to 38°C" and "from 35°C to 38°C", respectively. Applicants believe that the claims as amended clearly set forth that the specified temperature is in the range of 36°C to 38°C (for claim 14) and in the range of 35°C to 38°C (for claim 15).

Claims 1-4 were rejected under 35 U.S.C. 112, first paragraph, as allegedly not reasonably providing enablement for the production of any type of virus.

Without admitting to the propriety of the rejection, Applicants have canceled claims 1-4. Accordingly, the rejection is moot.

For the above reasons, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 112.

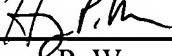
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CONCLUSION

Applicants believe the claims are in condition for allowance. An early indication of the same is requested. The Examiner is invited to contact Applicants' Attorney at the telephone number given below, if such would expedite the allowance of this application.

Respectfully submitted,

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